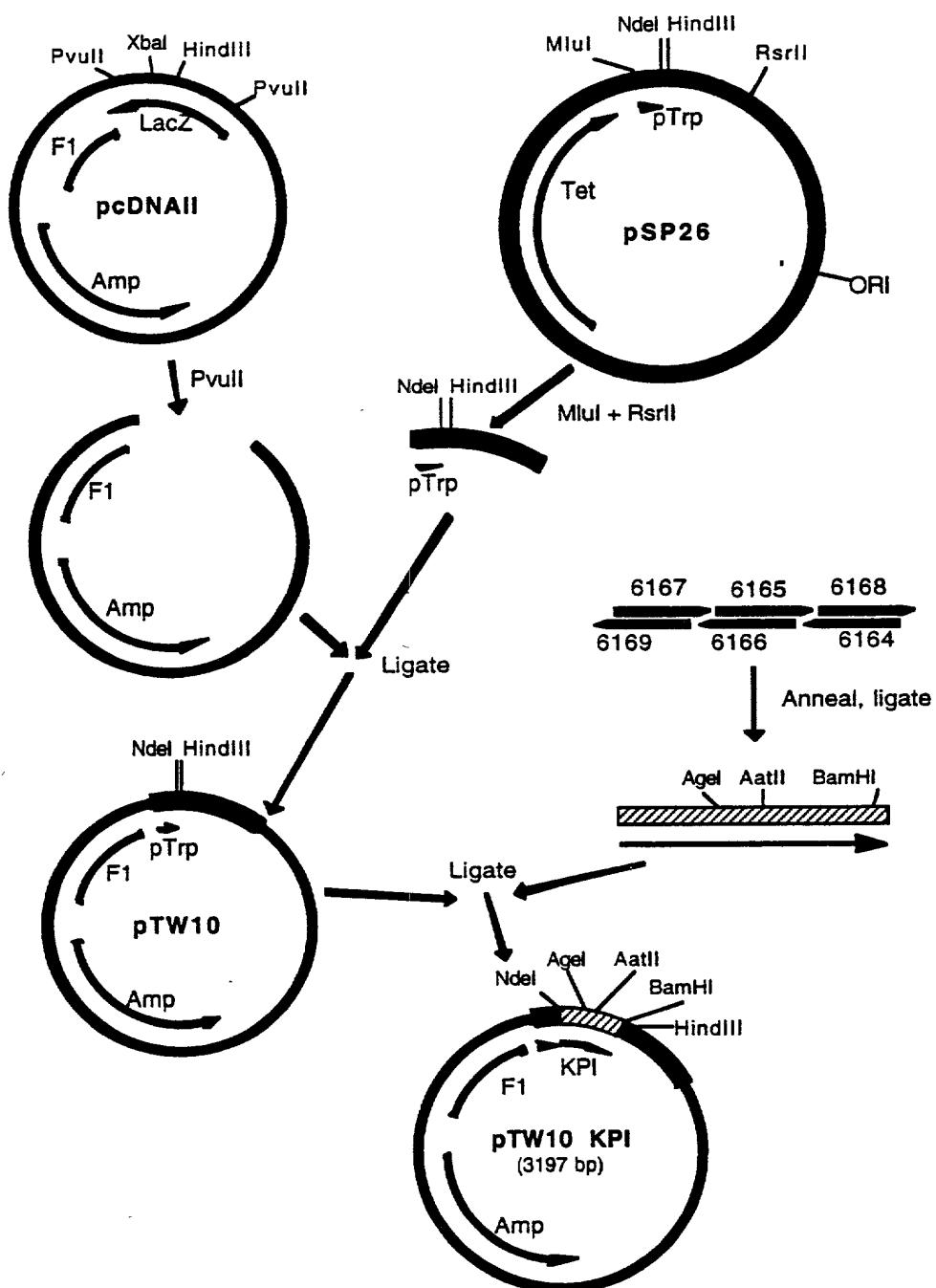


Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 1



Title: PROTEASE INHIBITOR
PEPTIDES

Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 2

Ndel

TATG AAA CAA AGC ACT ATT GCA CTG GCA CTC TTA CCG TTA CTG TTT ACC CCT GTG ACA AAA
AC TTT GTT TCG TGA TAA CGT GAC CGT GAG AAT GGC AAT GAC AAA TGG GGA CAC TGT TTT
►Met Lys Gln Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr Pro Val Thr Lys

KPI

AgeI

GCC GAG GTG TGC TCT GAA CAA GCT GAG ACC GGT CCG TGC CGT GCA ATG ATC TCC CGC TGG
CGG CTC CAC ACG AGA CTT GTT CGA CTC TGG CCA GGC ACG GCA CGT TAC TAG AGG GCG ACC
►Ala Glu Val Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg Ala Met Ile Ser Arg Trp

AatII

TAC TTT GAC GTC ACT GAA GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC
ATG AAA CTG CAG TGA CTT CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG
►Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Asn

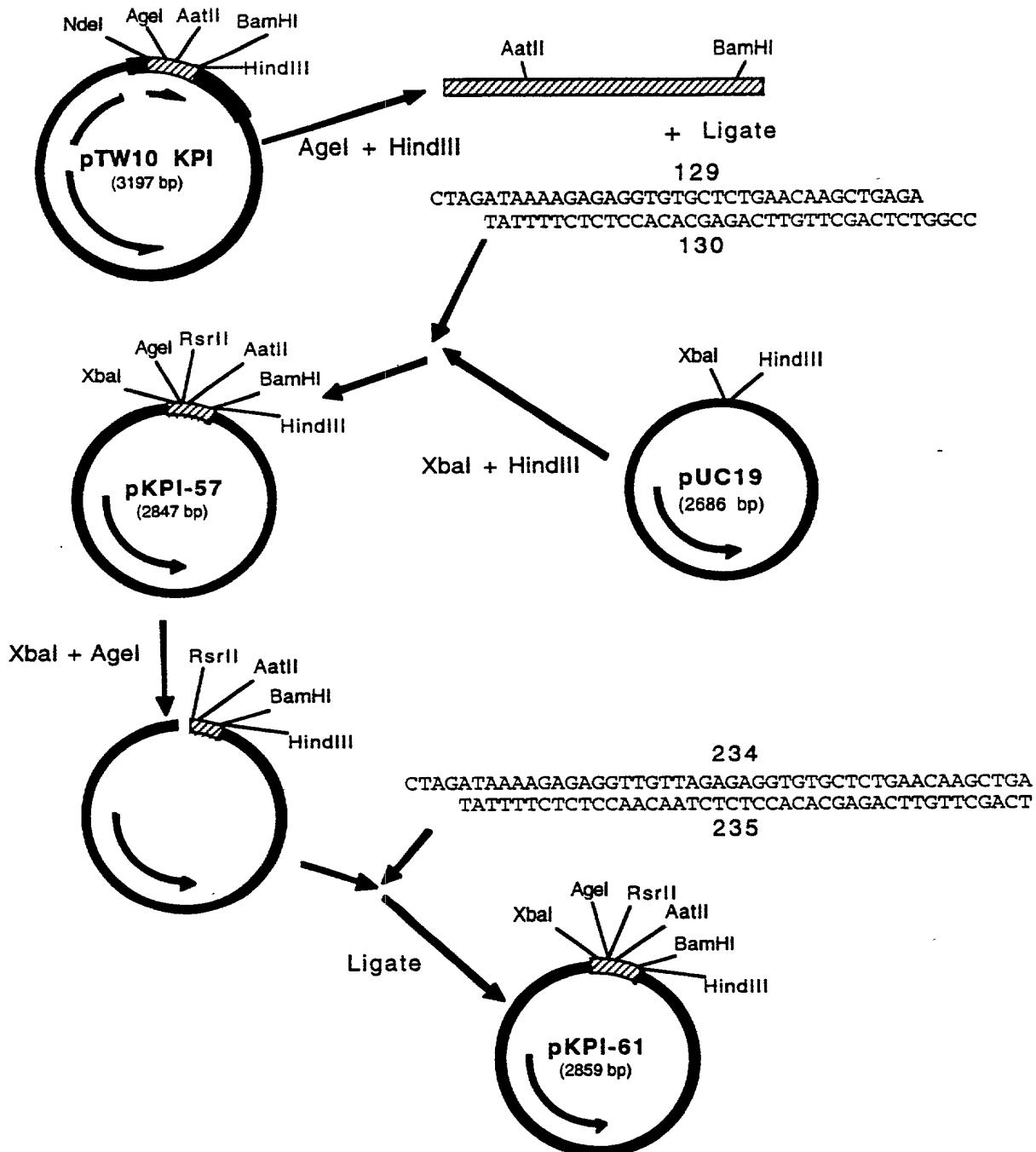
BamHI

HindIII

CGT AAC AAC TTT GAC ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TA
GCA TTG TTG AAA CTG TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA
►Arg Asn Asn Phe Asp Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

100025604-001-00000

Figure 3



Title: PROTEASE INHIBITOR

PEPTIDES

Inventor(s): R. Tyler WHITE et al

Appl. No.: 09/201,715

Figure 4

XbaI	KPI (1-57)	RsrII
		AgeI
CTA GAT AAA AGA	GAG GTG TGC TCT GAA CAA GCT GAG ACC GGT CCG TGC CGT	
TA TTT TCT	CTC CAC ACG AGA CTT GTT CGA CTC TGG CCA GGC ACG GCA	
► Leu Asp Lys Arg	Glu Val Cys Ser Glu Glu Ala Glu Thr Gly Pro Cys Arg	

AatII

GCA ATG ATC TCC CGC TGG TAC TTT GAC GTC ACT GAA GGT AAG TGC GCT CCA
CGT TAC TAG AGG GCG ACC ATG AAA CTG CAG TGA CTT CCA TTC ACG CGA GGT
►Ala Met Ile Ser Arg Trp Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro

TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC ACT GAA GAG
 AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG TGA CTT CTC
 ▶ Phe Phe Tyr Glu Glu Cys Glu Glu Asn Arg Asn Asn Phe Asp Thr Glu Glu

												BamHI	HindIII
TAC	TGC	ATG	GCA	GTG	TGC	GGA	TCC	GCT	ATT	TA			
ATG	ACG	TAC	CGT	CAC	ACG	CCT	AGG	CGA	TAA	ATT	CGA		
► Tyr Cys Met Ala Val Cys Gly Ser Ala Ile													

**Title: PROTEASE INHIBITOR
PEPTIDES**

Inventor(s): R. Tyler WHITE et al

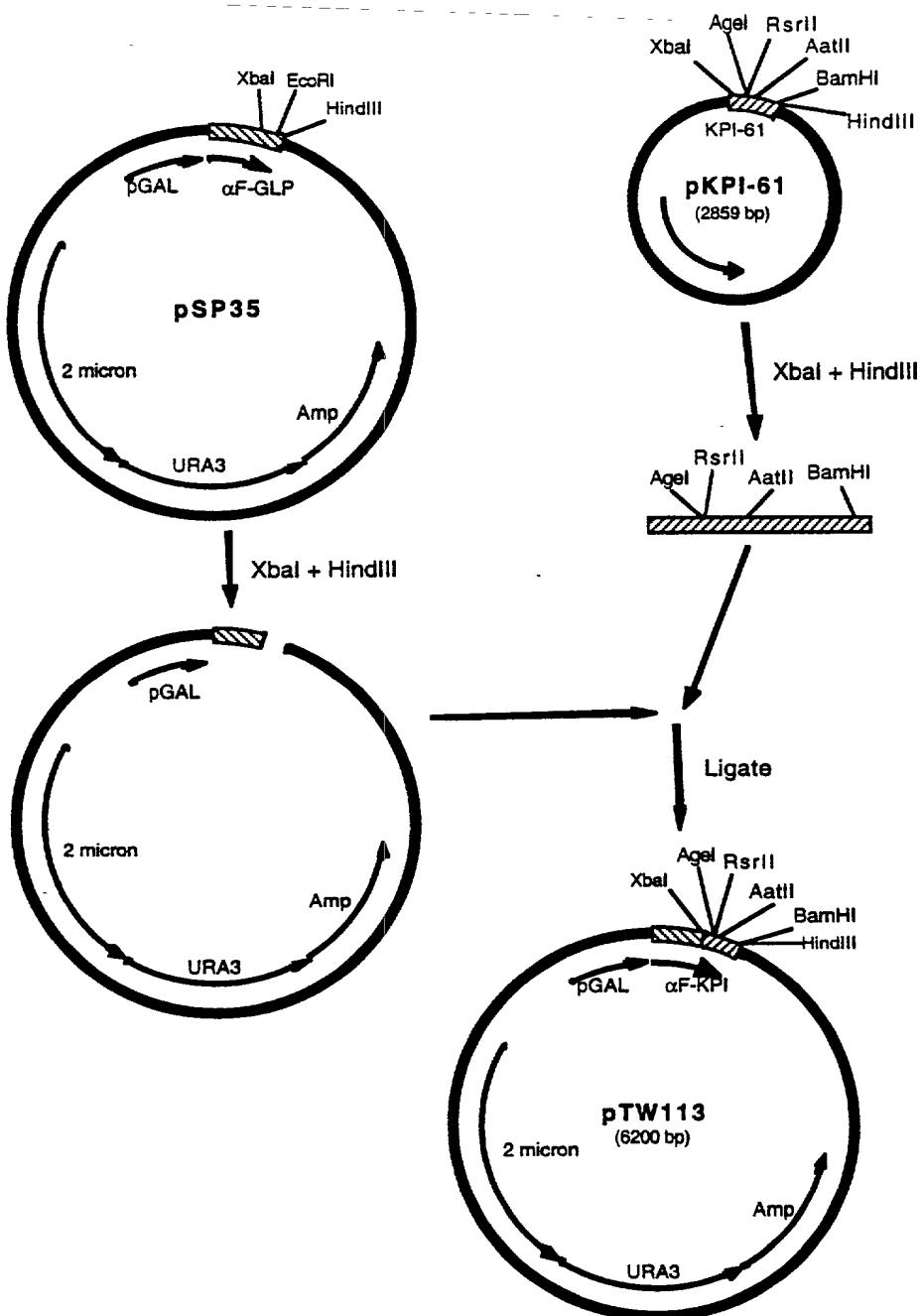
Appl. No.: 09/201,715

Figure 5

XbaI	KPI (-4-57)	RsrII
▶ Leu Asp Lys Arg	Glu Val Val Arg Glu Val Cys Ser Glu Gln Ala Glu Thr Gly	Argel
▶ Pro Cys Arg Ala Met Ile Ser Arg Trp Tyr Phe Asp Val Thr Glu Gly Lys Cys		
▶ Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp Thr Glu		
AatII		
GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TA		
CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA		
▶ Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile		
BamHI		
GCT CCA TTC TTT TAC CGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC ACT GAA		
CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG TGA CTT		
▶ Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp Thr Glu		
HindIII		

Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 6



10036604 021902

Title: PROTEASE INHIBITOR
PEPTIDES

Inventor(s): R. Tyler WHITE et al.

Appl. No.: 09/201,715

Figure 7

α -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA
► Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA AGC GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG
► Ala Pro Val Asn Thr Thr Glu Asp Glu Thr Ala Glu Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG
► Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT
► Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT
► Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Glu

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA ATG ATC TCC CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT TAC TAG AGG GCG ACC ATG AAA CTG CAG TGA CTT
► Ala Glu Thr Gly Pro Cys Arg Ala Met Ile Ser Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG
► Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A
► Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

10076604-024.902

Title: PROTEASE INHIBITOR PEPTIDES

Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 8

KPI (-4-57)

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Met - Ile - Ser - Arg
 8 9 10 11 12 13 14 15 16 17 18

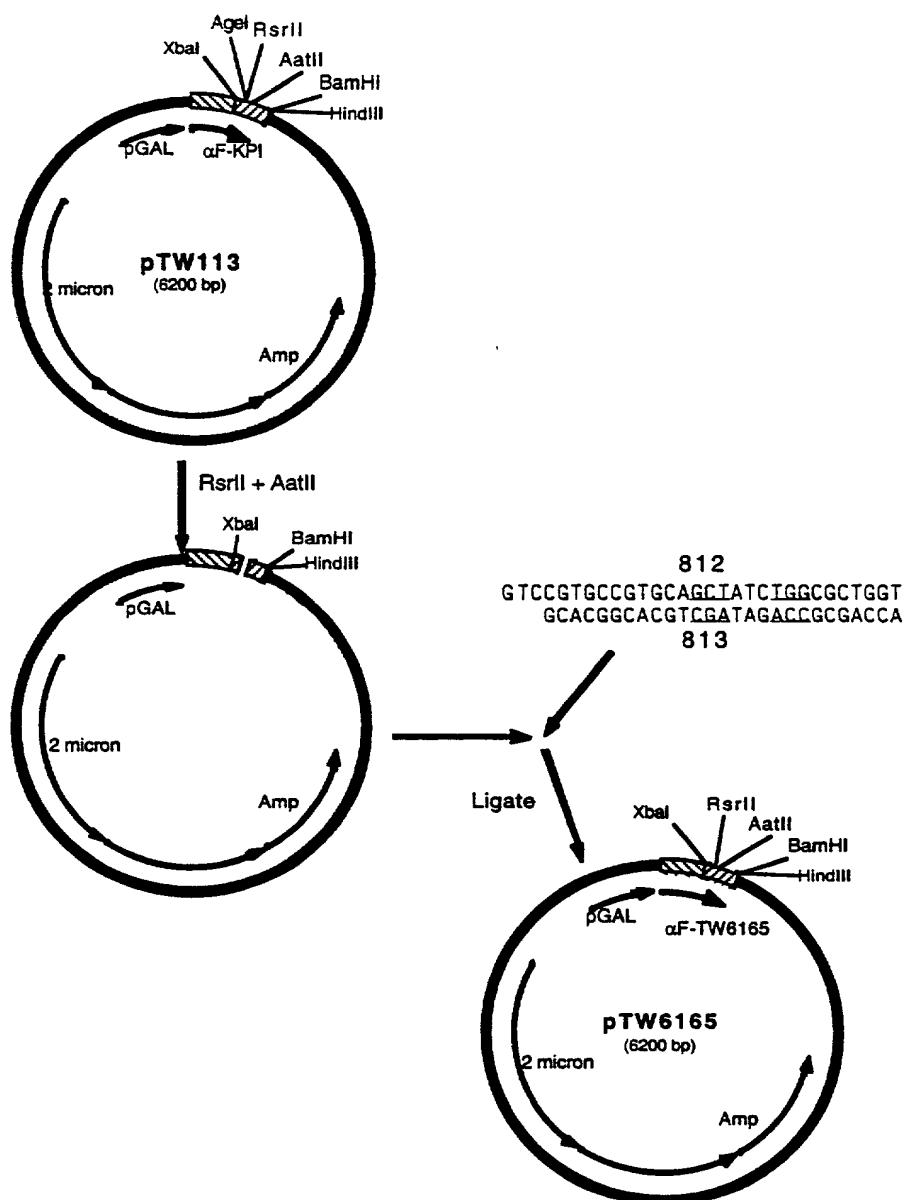
Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
 30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57

Figure 9



Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 10

pTW 6165

α -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA
►Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG
►Ala Pro Val Asn Thr Thr Glu Asp Glu Thr Ala Gin Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG
►Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT
►Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15A; S17W)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT
►Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gin

RsrII

AgeI

GCT GAG ACC GGT CCG TGC CGT GCA GCT ATC TGG CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT QGA TAG ACC GCG ACC ATG AAA CTG CAG TGA CTT
►Ala Glu Thr Gly Pro Cys Arg Ala Ala Ile Trp Arg Trp Tyr Phe Asp Val Thr Glu

AatII

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG
►Gly Lys Cys Ala Pro Phe Phe Tyr Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A
►Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

100076604-0011900E

Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 11

812
GTCCGTGCCGTGCAGCIATC~~I~~GGCGCTGGTACTTTGACGT
GCACGGCACGT~~G~~ATAGA~~G~~ACCGCGACCATGAAAC pTW6165 KPI(-4-57; M15A, S17F)
813
814
GTCCGTGCCGTGCAGCIATC~~I~~ACC~~G~~GCTGGTACTTTGACGT
GCACGGCACGT~~G~~ATAGA~~G~~ACCGCGACCATGAAAC pTW6166 KPI(-4-57; M15A, S17Y)
815
867
GTCCGTGCCGTGC~~A~~TTGATC~~I~~CCGCTGGTACTTTGACGT
GCACGGCACGT~~A~~ACTAGA~~G~~ACCGCGACCATGAAAC pTW6175 KPI(-4-57; M15L, S17F)
868
1493
GTCCGTGCCGTGC~~A~~TTGATC~~I~~ACC~~G~~GCTGGTACTTTGACGT
GCACGGCACGT~~A~~ACTAGA~~G~~ACCGCGACCATGAAAC pBG028 KPI(-4-57; M15L, S17Y)
1494
925
GTCCGTGCCGTGCAATGC~~A~~CT~~I~~CCGCTGGTACTTTGACGT
GCACGGCACGT~~A~~CTG~~G~~AAAGGCACCATGAAAC pTW6183 KPI(-4-57; I16H, S17F)
926
927
GTCCGTGCCGTGCAATGC~~A~~CT~~I~~ACC~~G~~GCTGGTACTTTGACGT
GCACGGCACGT~~A~~CTG~~G~~AAAGGCACCATGAAAC pTW6184 KPI(-4-57; I16H, S17Y)
928
929
GTCCGTGCCGTGCAATGC~~A~~CT~~I~~GGCGCTGGTACTTTGACGT
GCACGGCACGT~~A~~CTG~~G~~ACCGCGACCATGAAAC pTW6185 KPI(-4-57; I16H, S17W)
930
863
GTCCGTGCCGTGCAGCTCACT~~CC~~CGCTGGTACTTTGACGT
GCACGGCACGT~~G~~AGTGAGGGCGACCATGAAAC pTW6173 KPI(-4-57; M15A, I16H)
864
865
GTCCGTGCCGTGC~~A~~TTGCACT~~CC~~CGCTGGTACTTTGACGT
GCACGGCACGT~~A~~ACGT~~G~~AGGGCGACCATGAAAC pTW6174 KPI(-4-57; M15L, I16H)
866

Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 12

pTW 6166

α -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA
►Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG
►Ala Pro Val Asn Thr Thr Glu Asp Glu Thr Ala Gin Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG
►Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCC TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT
►Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15A, S17Y)

GAA GAA GGG GTC TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT
►Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gin

RsrII

AgeI

GCT GAG ACC GGT CCG TGC CGT GCA GCT ATC TAC CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT CGA TAG ATG GCG ACC ATG AAA CTG CAG TGA CTT
►Ala Glu Thr Gly Pro Cys Arg Ala Ala Ile Tyr Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CGG CCA ACG CGG CCG TTG GCA TTG TTG AAA CTG
►Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A
►Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 13

pTW 6175

α -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA
►Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG
►Ala Pro Val Asn Thr Thr Glu Asp Glu Thr Ala Gin Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG
►Ile G y Tyr Leu Asp Leu Glu G y Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT
►Ser Thr Asn Asn G y Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15L, S17F)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT
►Glu Glu G y Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA TTG ATC TTC CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT AAC TAG AAG GCG ACC ATG AAA CTG CAG TGA CTT
►Ala Glu Thr G y Pro Cys Arg Ala Leu Ile Phe Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG
►Gly Lys Cys Ala Pro Phe Phe Tyr G y G y Cys Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A
►Thr Glu Glu Tyr Cys Met Ala Val Cys Glu Ser Ala Ile

Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 14

pBG028

α -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA
► Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG
► Ala Pro Val Asn Thr Thr Glu Asp Glu Thr Ala Gin Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG
► Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC ACC ATT GCT GCT AAA
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT
► Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

KPI(-4-57; M15L, S17Y)

XbaI GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT
► Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gin

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA TTG ATC TAC CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT AAC TAG ATG GCG ACC ATG AAA CTG CAG TGA CTT
► Ala Glu Thr Gly Pro Cys Arg Ala Leu Ile Tyr Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG
► Gly Lys Cys Ala Pro Phe Phe Tyr Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A
► Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

10036604-021902

Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 15

pTW6183

α -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA
►Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG
►Ala Pro Val Asn Thr Thr Glu Asp Glu Thr Ala Gin Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG
►Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT
►Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

KPI(-4-57; I16H, S17F)

XbaI

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT
►Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Glu

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA ATG CAC TTC CCC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT TAC GTG AAG GCG ACC ATG AAA CTG CAG TGA CTT
►Ala Glu Thr Gly Pro Cys Arg Ala Met His Phe Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG
►Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A
►Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

4000766004 Oct 1992

Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 16

pTW6184

α -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA
►Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG
►Ala Pro Val Asn Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG
►Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA CTT
►Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; I16H, S17Y)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT
►Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

GCT GAG ACC GGT CCG TGC CGT GCA ATG CAC TAC CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT TAC GTG ATG CGC ACC ATG AAA CTG CAG TGA CTT
►Ala Glu Thr Gly Pro Cys Arg Ala Met His Tyr Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CGG CCG TTG GCA TTG TTG AAA CTG
►Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Oys Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG CCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A
►Thr Glu Glu Tyr Cys Met Ala Val Cys Glu Ser Ala Ile

1000766004-024902

Title: PROTEASE INHIBITOR
PEPTIDES

Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 17

pTW6185

α -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA
►Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG
►Ala Pro Val Asn Thr Thr Glu Asp Glu Thr Ala Glu Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG
►Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT
►Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI KPI(-4-57; I16H, S17W)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT
►Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Glu

RsrII

AgeI

GCT GAG ACC GGT CCG TGC CGT GCA ATG CAC TGG CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT TAC GTG ACC GCG ACC ATG AAA CTG CAG TGA CTT
►Ala Glu Thr Gly Pro Cys Arg Ala Met His Trp Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG
►Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Asn Arg Asn Asn Phe Asp

AatII

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A
►Thr Glu Glu Tyr Cys Met Ala Val Cys Glu Ser Ala Ile

100236604 021902

Title: PROTEASE INHIBITOR
PEPTIDES

Inventor(s): R. Tyler WHITE et al.

Appl. No.: 09/201,715

Figure 18

pTW6173

α -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA
► Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG
► Ala Pro Val Asn Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Gu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG
► Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC CGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT
► Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15A, I16H)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT
► Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA GCT CAC TCC CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT CGA GTG AGG GGG ACC ATG AAA CTG CAG TGA CTT
► Ala Glu Thr Gly Pro Cys Arg Ala Ala His Ser Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CGG CGG TTG GCA TTG TTG AAA CTG
► Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A
► Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

10026504-0024502

Title: PROTEASE INHIBITOR
PEPTIDES

Inventor(s): R. Tyler WHITE et al.

Appl. No.: 09/201,715

Figure 19

pTW6174

α -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA
►Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TIG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG
►Ala Pro Val Asn Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG
►Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCG TGT TTA TIG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT
►Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15L, 116H)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT
►Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC CGT CCG TGC CGT GCA TTG CAC TCC CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT AAC GTG AGG GCG ACC ATG AAA CTG CAG TGA CTT
►Ala Glu Thr Gly Pro Cys Arg Ala Leu His Ser Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CGG CCG TTG GCA TTG TTG AAA CTG
►Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A
►Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

4039620-4221982

Title: PROTEASE INHIBITOR

PEPTIDES

Inventor(s): R. Tyler WHITE et al.

Appl. No.: 09/201,715

Figure 20

KPI (-4-57; M15A, S17W) TW6165

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
 -4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Ala - Ile - Trp - Arg
 8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
 19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
 30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57

Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 21

KPI(-4-57; M15A, S17Y) TW6166

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Ala - Ile - Tyr - Arg
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57

Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 22

KPI(-4-57; M15L, S17F) TW6175

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Leu - Ile - Phe - Arg
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57

400026604 - 02216026

Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 23

KPI(-4-57; M15L, S17Y) BG028

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Leu - Ile - Tyr - Arg
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57

100076604-022902

Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 24

KPI(-4-57; I16H, S17F) TW6183

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Met - His - Phe - Arg
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57

1000266004-021902

Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 25

KPI(-4-57; I16H, S17Y) TW6184

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Met - His - Tyr - Arg
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57

4000565047-021802

Title: PROTEASE INHIBITOR
PEPTIDES

Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 26

KPI(-4-57; I16H, S17W) TW6185

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Met - His - Tyr - Arg
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57

Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 27

KPI(-4-57; M15A, S17F) DD185

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Ala - Ile - Phe - Arg
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57

100075504-001-0002

Title: PROTEASE INHIBITOR
PEPTIDES

Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 28

KPI(-4-57; M15A, I16H) TW6173

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Ala - His - SerTrp - Arg
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57

Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 29

KPI(-4-57; M15L, I16H) TW6174

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Leu - His - Ser - Arg
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57

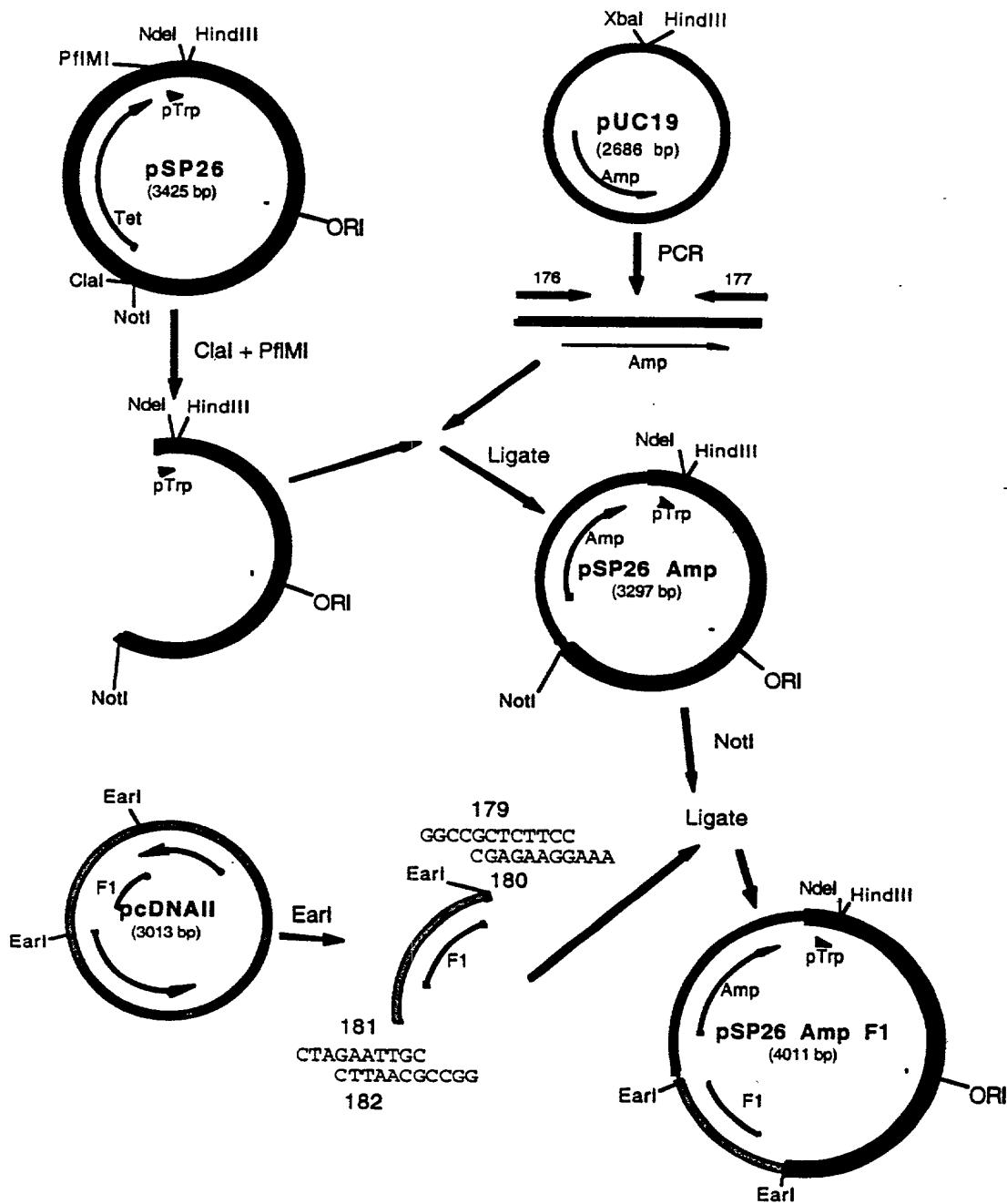
100076604 - DELETION

Title: PROTEASE INHIBITOR
PEPTIDES

Inventor(s): R. Tyler WHITE et al.

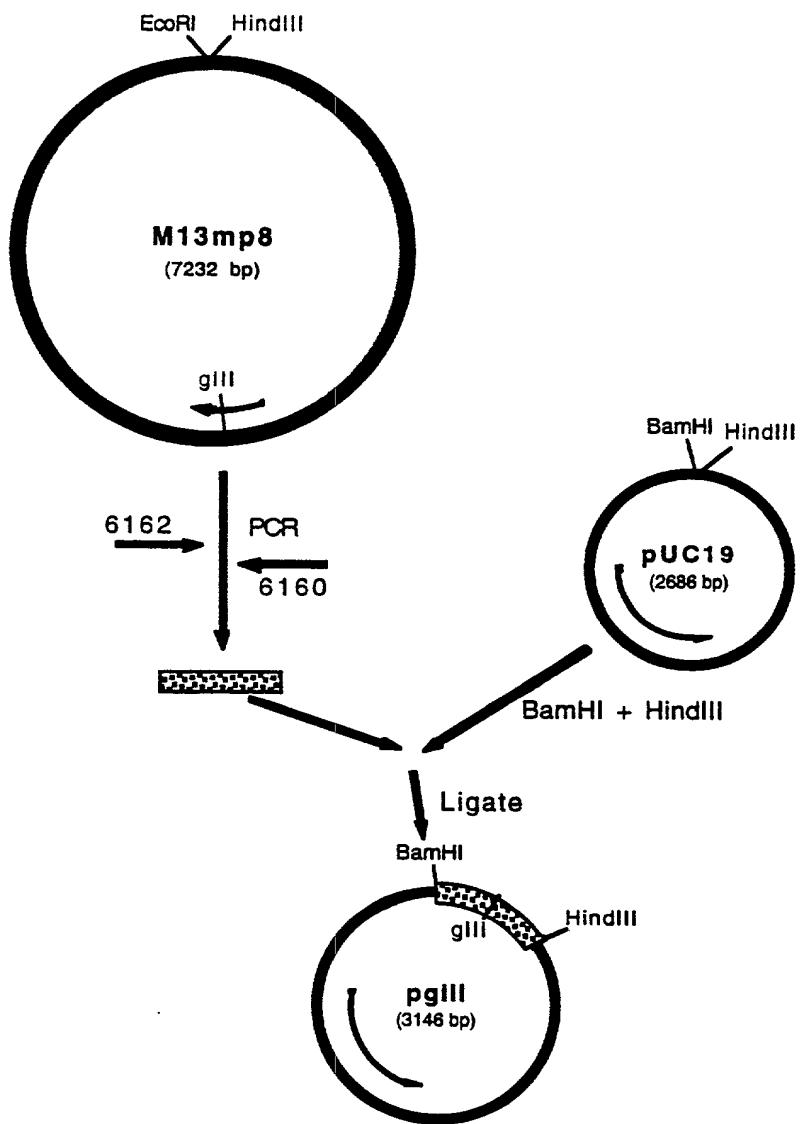
Appl. No.: 09/201,715

Figure 30



Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 31

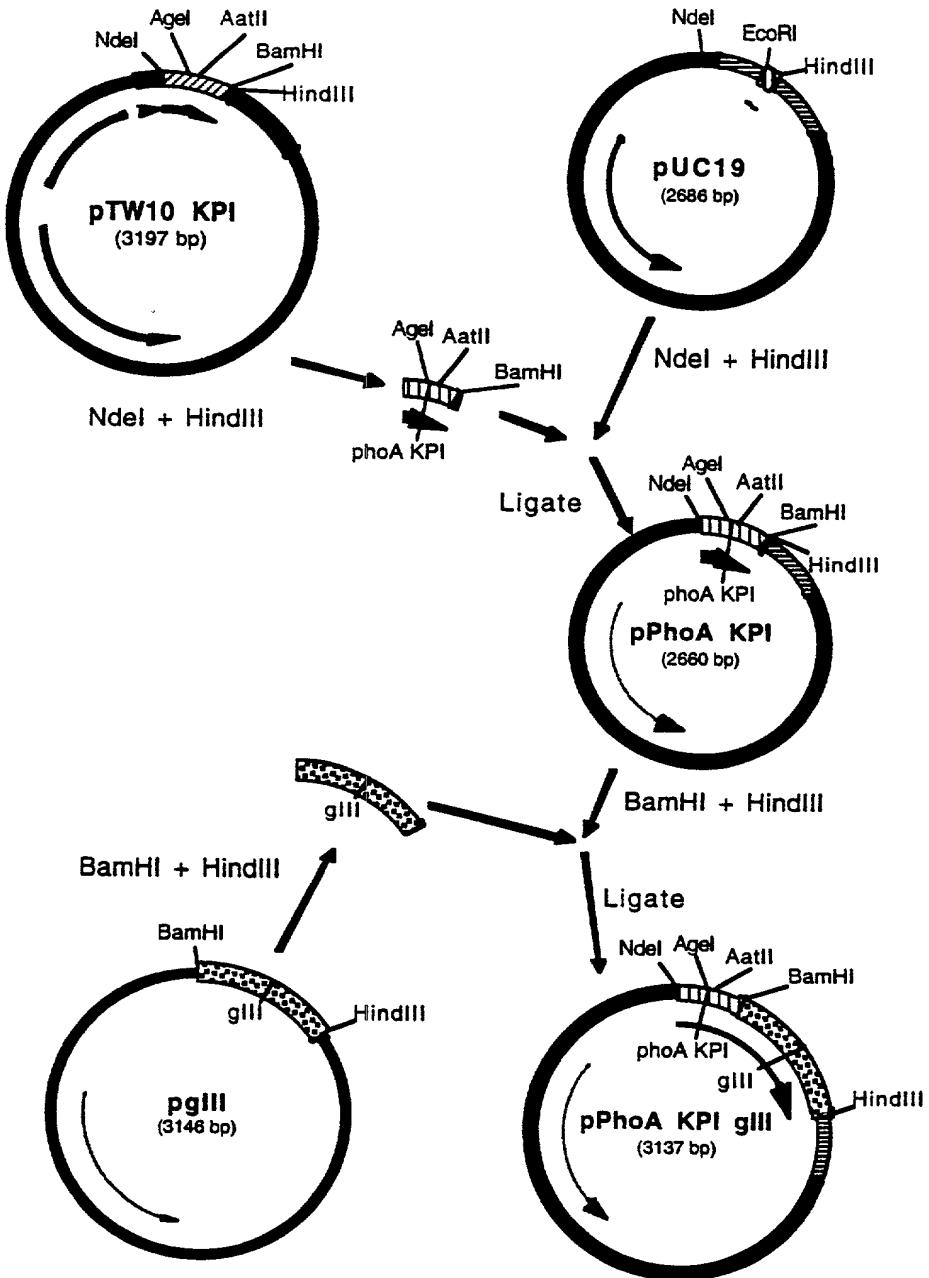


Title: PROTEASE INHIBITOR
PEPTIDES

Inventor(s): R. Tyler WHITE et al.

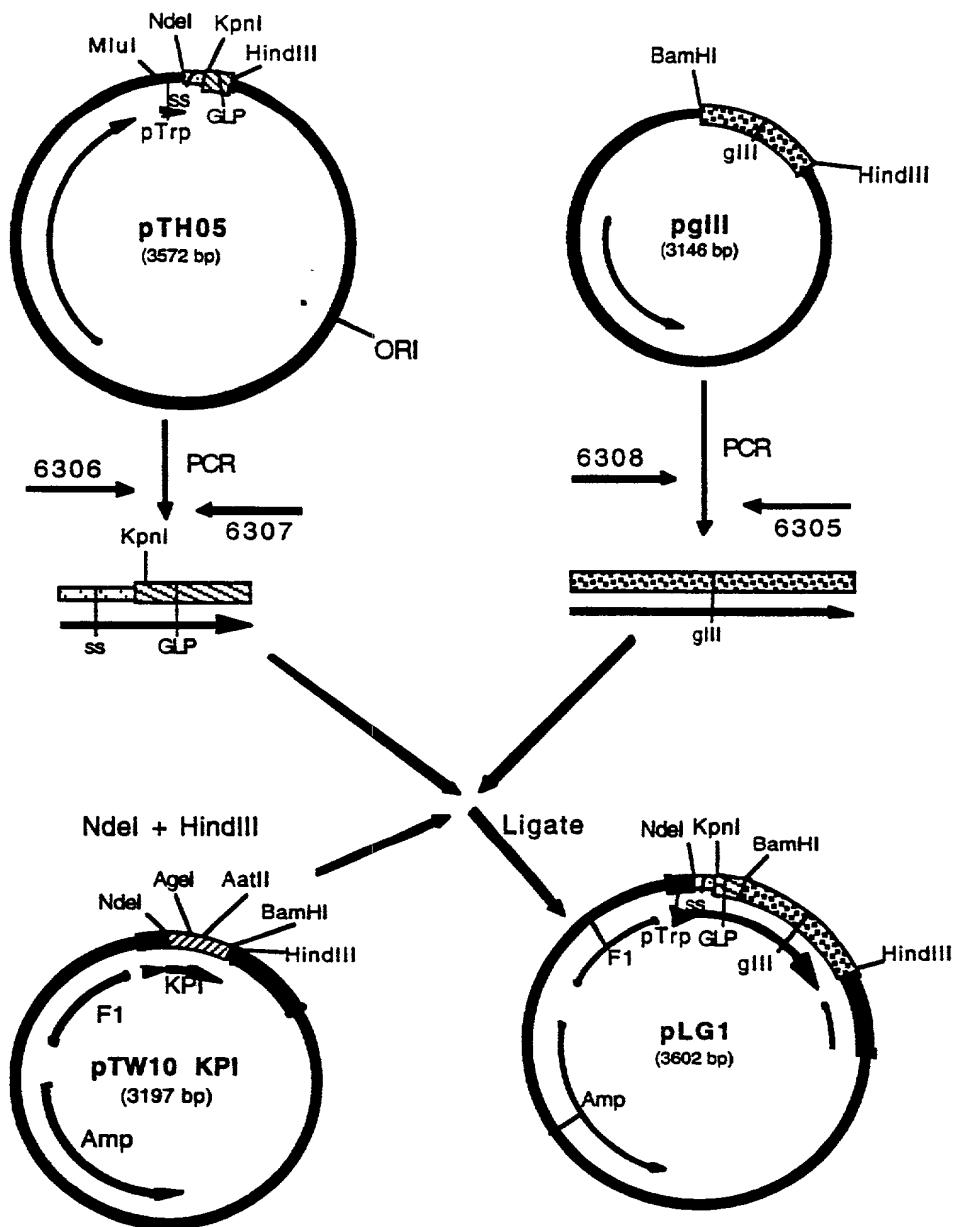
Appl. No.: 09/201,715

Figure 32



Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

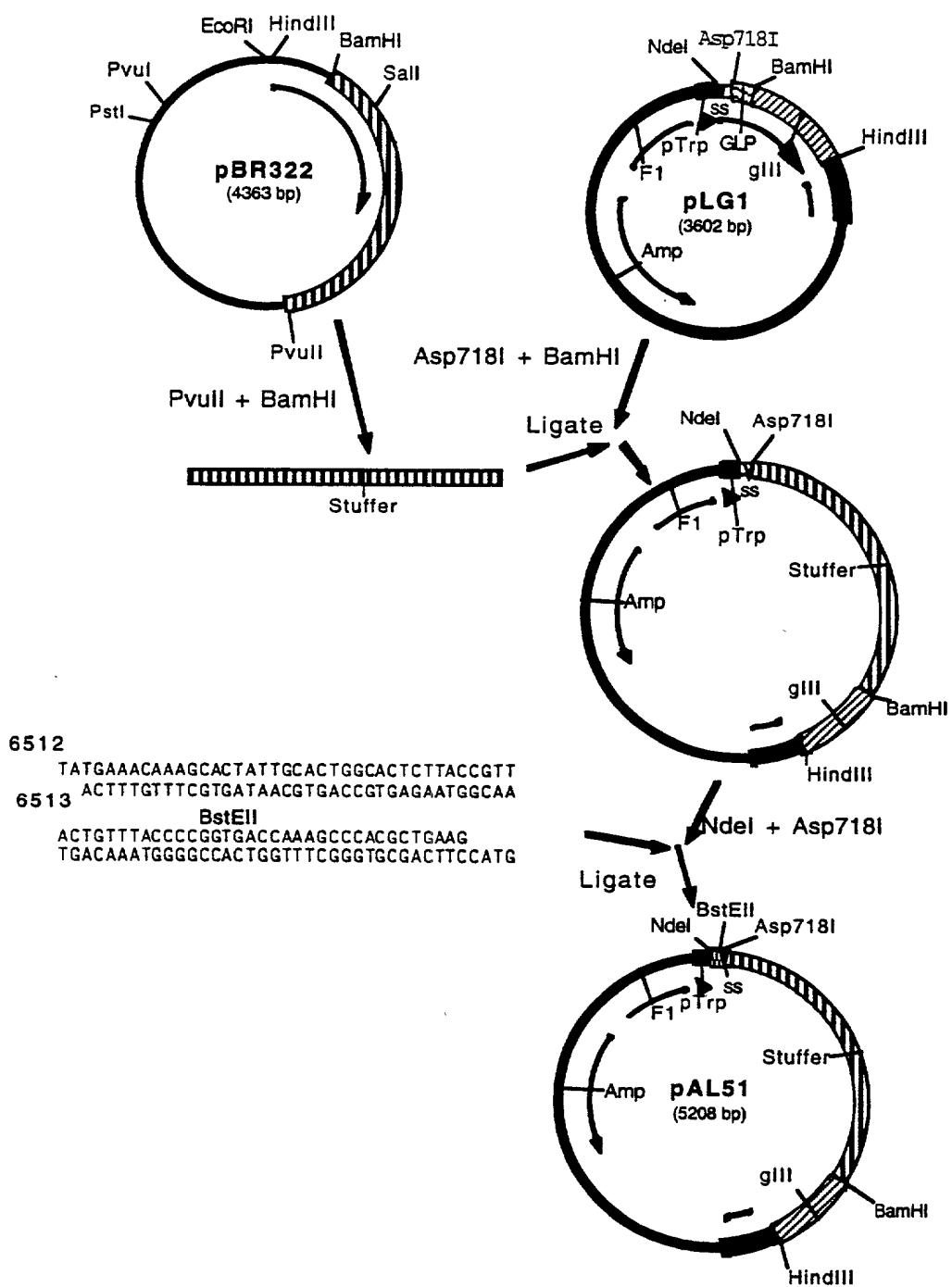
Figure 33



Title: PROTEASE INHIBITOR
PEPTIDES

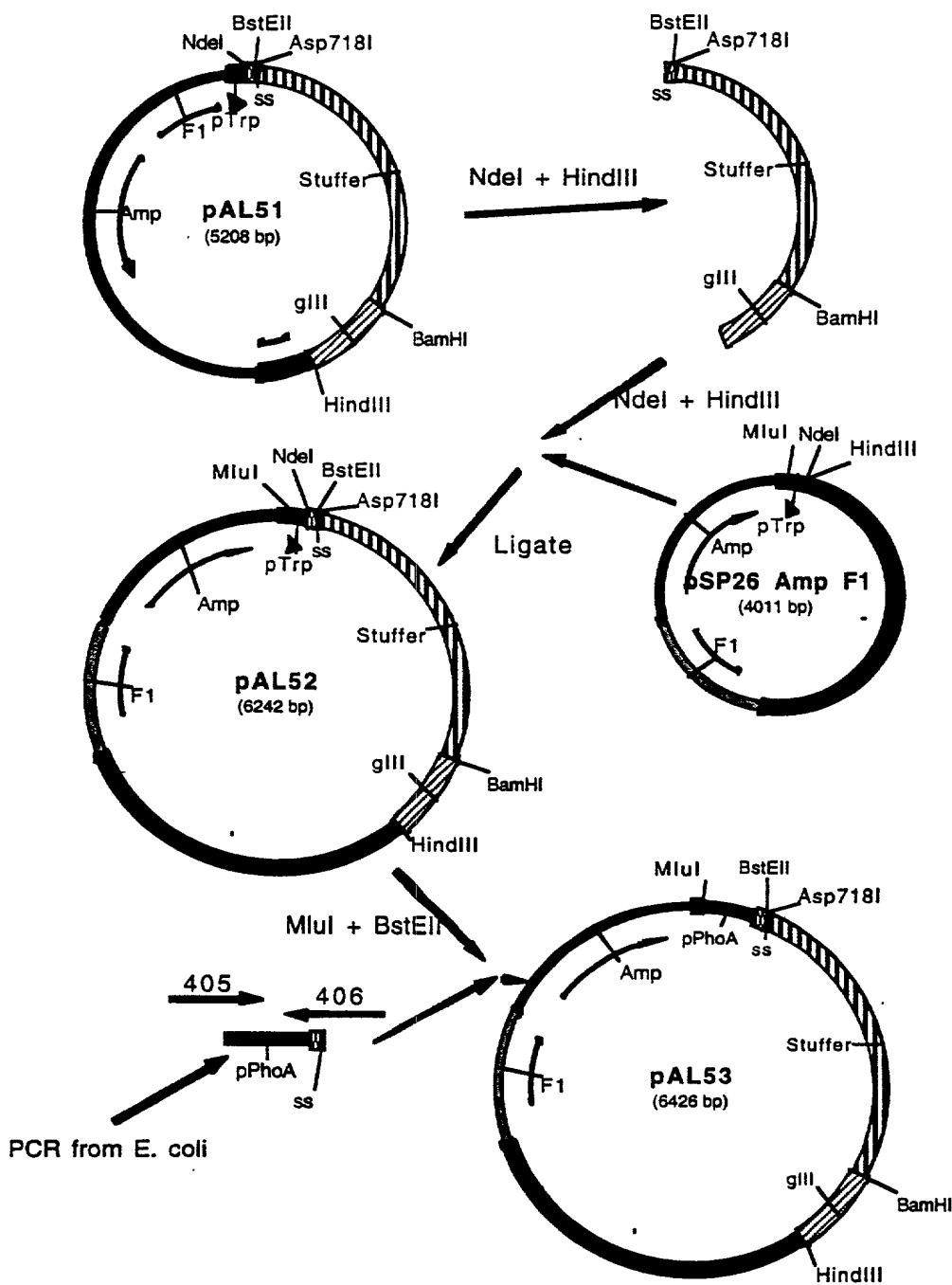
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 34



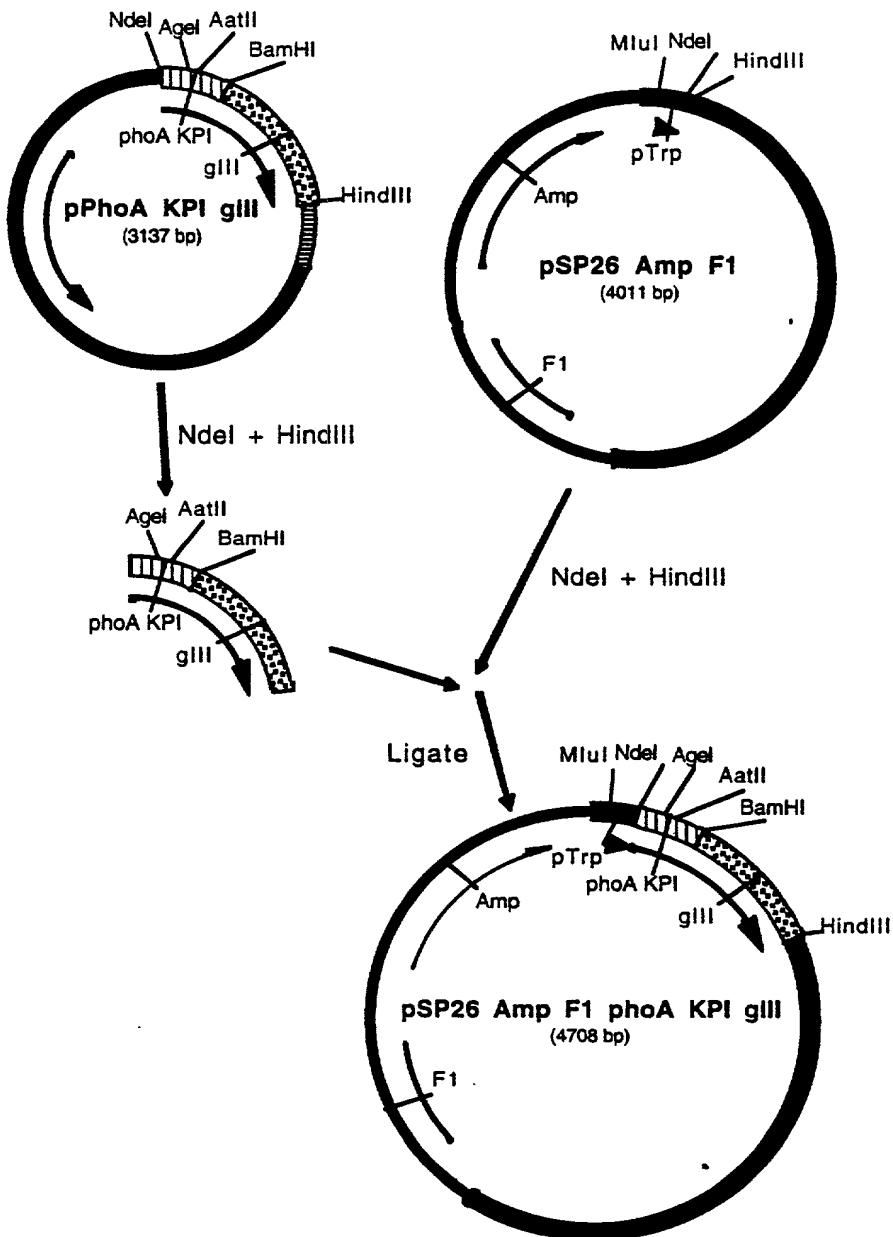
Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 35



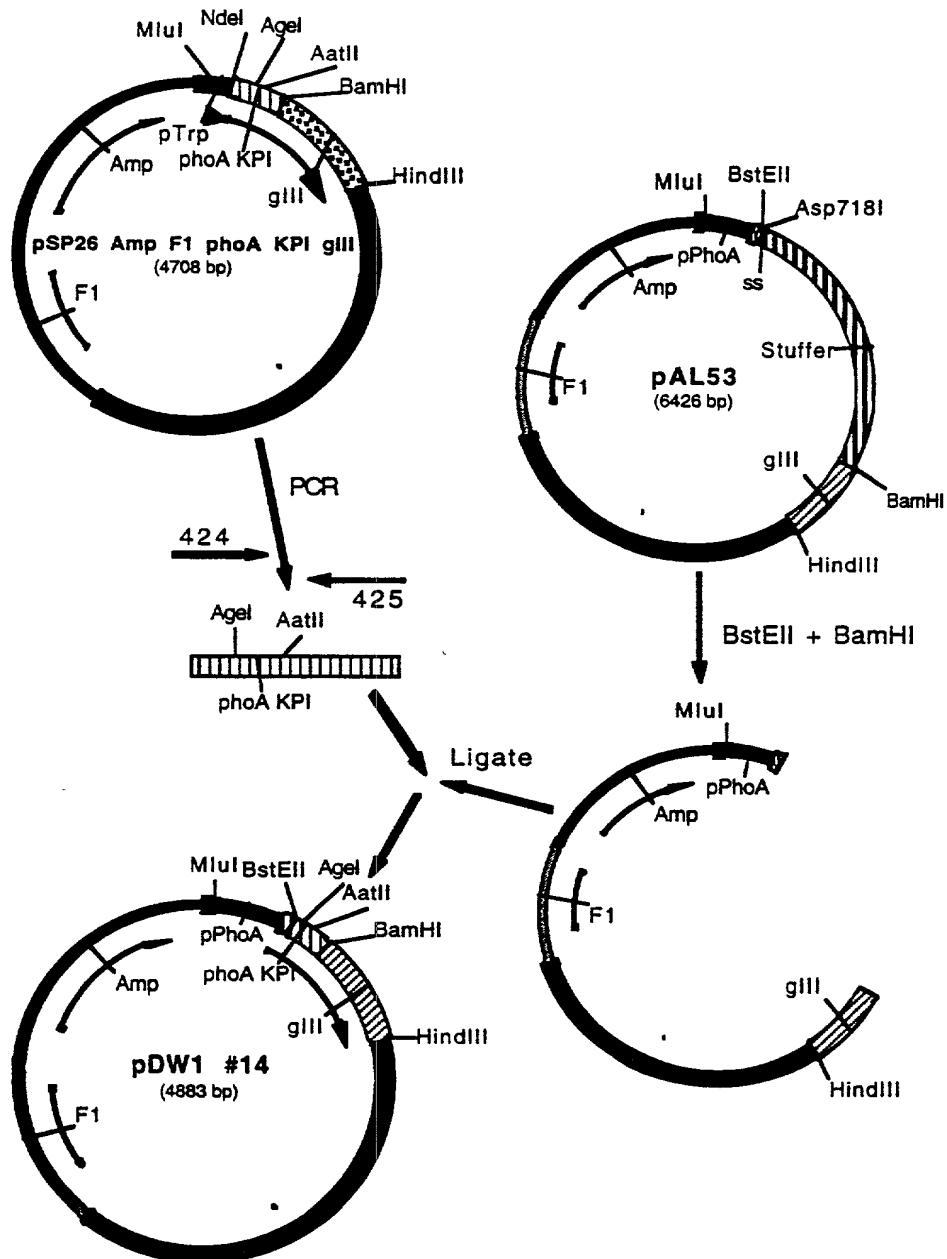
Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 36



Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 37



Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 38

phoA signal → BstEII
GTG AAA CAA AGC ACT ATT GCA CTG GCA CTC TTA CCG TTA CTG TTT ACC CCG GTG ACC AAA
► Val Lys Gln Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr Pro Val Thr Lys

KPI (1-55) → Agel
GCC GAG GTG TGC TCT GAA CAA GCT GAG ACC GGT CCG TGC CGT GCA ATG ATC TCC CGC TGG
► Ala Glu Val Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg Ala Met Ile Ser Arg Trp

AatII
TAC TTT GAC GTC ACT GAA GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC
► Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Asn

BamHI → gIII
CGT AAC AAC TTT GAC ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GGT GGT GGC TCT
► Arg Asn Asn Phe Asp Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Gly Gly Gly Ser

GGT TCC GGT GAT TTT GAT TAT GAA AAG ATG GCA AAC GCT AAT AAG GGG GCT ATG ACC GAA
► Gly Ser Gly Asp Phe Asp Tyr Glu Lys Met Ala Asn Ala Asn Lys Gly Ala Met Thr Glu

AAT GCC GAT GAA AAC GCG CTA CAG TCT GAC GCT AAA GGC AAA CTT GAT TCT GTC GCT ACT
► Asn Ala Asp Glu Asn Ala Leu Gln Ser Asp Ala Lys Gly Lys Leu Asp Ser Val Ala Thr

GAT TAC GGT GCT ATC GAT GGT TTC ATT GGT GAC GTT TCC GGC CTT GCT AAT GGT AAT
► Asp Tyr Gly Ala Ala Ile Asp Gly Phe Ile Gly Asp Val Ser Gly Leu Ala Asn Gly Asn

GGT GCT ACT GGT GAT TTT GCT GGC TCT AAT TCC CAA ATG GCT CAA GTC GGT GAC GGT GAT
► Gly Ala Thr Gly Asp Phe Ala Gly Ser Asn Ser Gln Met Ala Gln Val Gly Asp Gly Asp

AAT TCA CCT TTA ATG AAT AAT TTC CGT CAA TAT TTA CCT TCC CTC CCT CAA TCG GTT GAA
► Asn Ser Pro Leu Met Asn Asn Phe Arg Gln Tyr Leu Pro Ser Leu Pro Gln Ser Val Glu

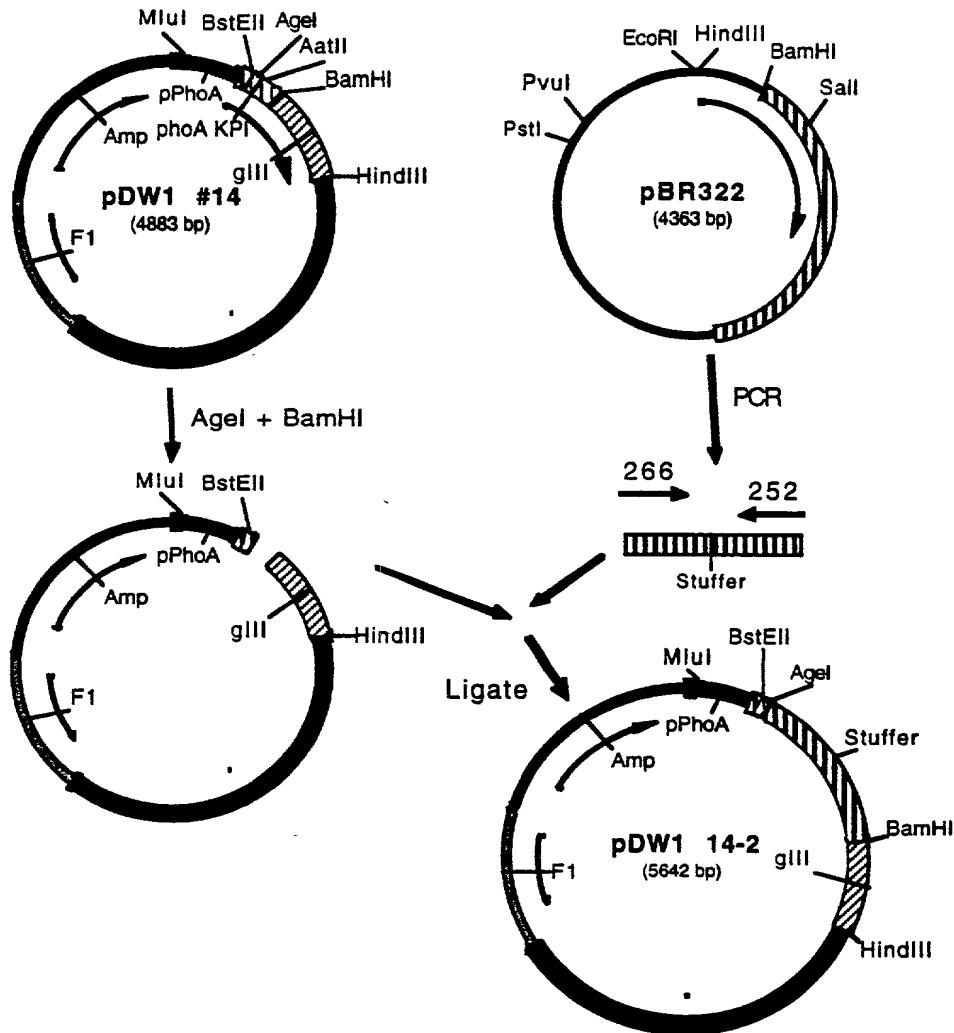
TGT CGC CCT TTT GTC TTT GGC GCT GGT AAA CCA TAC GAA TTT TCT ATT GAT TGT GAC AAA
► Cys Arg Pro Phe Val Phe Gly Ala Gly Lys Pro Tyr Glu Phe Ser Ile Asp Cys Asp Lys

ATA AAC TTA TTC CGT GGT GTC TTT GCG TTT CTT TTA TAT GTT GCC ACC TTT ATG TAT GTC
► Ile Asn Leu Phe Arg Gly Val Phe Ala Phe Leu Leu Tyr Val Ala Thr Phe Met Tyr Val

TTT TCT ACG TTT GCT AAC ATA CTG CGT AAT AAG GAG TCT TAA TA
► Phe Ser Thr Phe Ala Asn Ile Leu Arg Asn Lys Glu Ser •••

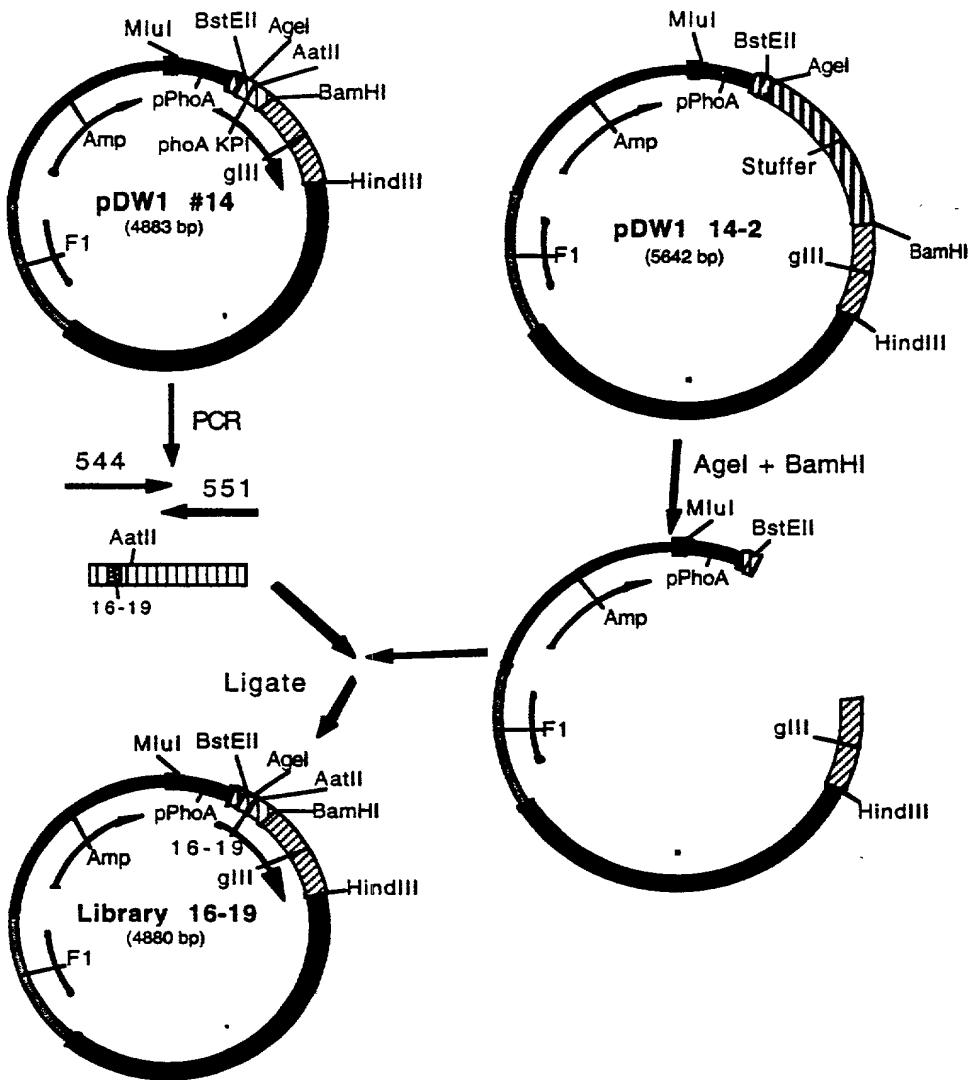
Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 39



Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 40



Title: PROTEASE INHIBITOR
PEPTIDES

Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 41

phoA signal → BstEII
GTG AAA CAA AGC ACT ATT GCA CTG GCA CTC TTA CCG TTA CTG TTT ACC CCG GTG ACC AAA
► Val Lys Gin Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr Pro Val Thr Lys
KPI (1-55; 16 - 19) → AgeI 16 - 19
GCC GAG GTG TGC TCT GAA CAA GCT GAG ACC GGT CCG TGC CGT NNS NNS NNS NNS TGG TAC
► Ala Glu Val Cys Ser Glu Gin Ala Glu Thr Gly Pro Cys Arg --- --- Trp Tyr
AatII
TTT GAC GTC ACT GAA GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT
► Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Asn Arg
BamHI gIII
AAC AAC TTT GAC ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GGT GGT GGC TCT GGT
► Asn Asn Phe Asp Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Gly Gly Ser Gly
TCC GGT GAT TTT GAT TAT GAA AAG ATG GCA AAC GCT AAT AAG GGG GCT ATG ACC AAC AAT
► Ser Gly Asp Phe Asp Tyr Glu Lys Met Ala Asn Ala Asn Lys Gly Ala Met Thr Glu Asn
GCC GAT GAA AAC GCG CTA CAG TCT GAC GCT AAA GGC AAA CTT GAT TCT GTC GCT ACT GAT
► Ala Asp Glu Asn Ala Leu Gin Ser Asp Ala Lys Gly Lys Leu Asp Ser Val Ala Thr Asp
TAC GGT GCT GCT ATC GAT GGT TTC ATT GGT GAC GTT TCC GGC CTT GCT AAT GGT AAT GGT
► Tyr Gly Ala Ala Ile Asp Gly Phe Ile Gly Asp Val Ser Gly Leu Ala Asn Gly Asn Gly
gIII
GCT ACT GGT GAT TTT GCT GGC TCT AAT TCC CAA ATG GCT CAA GTC GGT GAC GGT GAT AAT
► Ala Thr Gly Asp Phe Ala Gly Ser Asn Ser Gin Met Ala Gin Val Gly Asp Gly Asp Asn
TCA CCT TTA ATG AAT AAT TTC CGT CAA TAT TTA CCT TCC CTC CCT CAA TCG GTT GAA TGT
► Ser Pro Leu Met Asn Asn Phe Arg Gin Tyr Leu Pro Ser Leu Pro Gin Ser Val Glu Cys
CGC CCT TTT GTC TTT GGC GCT GGT AAA CCA TAC GAA TTT TCT ATT GAT TGT GAC AAA ATA
► Arg Pro Phe Val Phe Gly Ala Gly Lys Pro Tyr Glu Phe Ser Ile Asp Cys Asp Lys Ile
AAC TTA TTC CGT GGT GTC TTT GCG TTT CTT TTA TAT GTT GCC ACC TTT ATG TAT GTA TTT
► Asn Leu Phe Arg Gly Val Phe Ala Phe Leu Leu Tyr Val Ala Thr Phe Met Tyr Val Phe
TCT ACG TTT GCT AAC ATA CTG CGT AAT AAG GAG TCT TAA TA
► Ser Thr Phe Ala Asn Ile Leu Arg Asn Lys Glu Ser ...

Title: PROTEASE INHIBITOR
PEPTIDES

Inventor(s): R. Tyler WHITE et al.

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Figure 42

phoA signal

GTG AAA CAA AGC ACT ATT GCA CTG GCA CTC TTA CCG TTA CTG TTT ACC CCG GTG ACC AAA
► Val Lys Gin Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr Pro Val Thr Lys
KPI (1-55; M15A, S17F) BstEII

GCC GAG GTG TGC TCT GAA CAA GCT GAG ACC GGT CCG TGC CGT GCA GCT ATC TTC CGC TGG
► Ala Glu Val Cys Ser Glu Gin Ala Glu Thr Gly Pro Cys Arg Ala Ala Ile Phe Arg Trp Agl

TAC TTT GAC GTC ACT GAA GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC
► Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Oys Gly Asn AatII

CGT AAC AAC TTT GAC ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GGT GGT GGC TCT
► Arg Asn Asn Phe Asp Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Gly Gly Gly Ser BamHI

GGT TCC GGT GAT TTT GAT TAT GAA AAG ATG GCA AAC GCT AAT AAG GGG GCT ATG ACC GAA
► Gly Ser Gly Asp Phe Asp Tyr Glu Lys Met Ala Asn Ala Asn Lys Gly Ala Met Thr Glu

AAT GCC GAT GAA AAC GCG CTA CAG TCT GAC GCT AAA GGC AAA CTT GAT TCT GTC GCT ACT
► Asn Ala Asp Glu Asn Ala Leu Gin Ser Asp Ala Lys Gly Lys Leu Asp Ser Val Ala Thr

GAT TAC GGT GCT ATC GAT GGT TTC ATT GGT GAC GTT TCC GGC CTT GCT AAT GGT AAT
► Asp Tyr Gly Ala Ala Ile Asp Gly Phe Ile Gly Asp Val Ser Gly Leu Ala Asn Gly Asn

GGT GCT ACT GGT GAT TTT GCT GGC TCT AAT TCC CAA ATG GCT CAA GTC GGT GAC GGT GAT
► Gly Ala Thr Gly Asp Phe Ala Gly Ser Asn Ser Gin Met Ala Gin Val Gly Asp Gly Asp

AAT TCA CCT TTA ATG AAT TTC CGT CAA TAT TTA CCT TCC CTC CCT CAA TCG GTT GAA
► Asn Ser Pro Leu Met Asn Asn Phe Arg Gin Tyr Leu Pro Ser Leu Pro Gin Ser Val Glu

TGT CGC CCT TTT GTC TTT GGC GCT GGT AAA CCA TAC GAA TTT TCT ATT GAT TGT GAC AAA
► Cys Arg Pro Phe Val Phe Gly Ala Gly Lys Pro Tyr Glu Phe Ser Ile Asp Cys Asp Lys

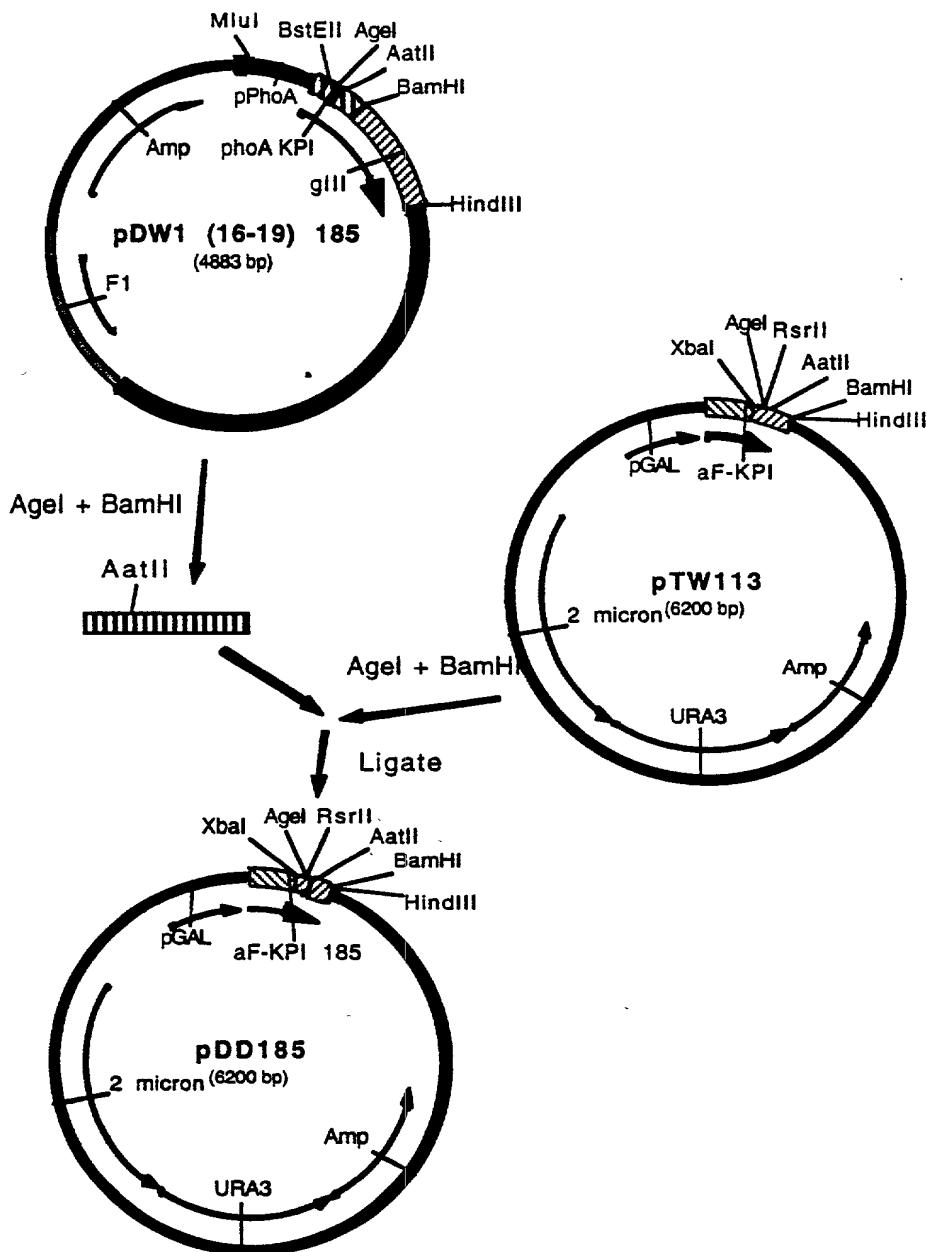
ATA AAC TTA TTC CGT GGT GTC TTT GCG TTT CTT TTA TAT GTT GCC ACC TTT ATG TAT GTA
► Ile Asn Leu Phe Arg Gly Val Phe Ala Phe Leu Leu Tyr Val Ala Thr Phe Met Tyr Val

TTT TCT ACG TTT GCT AAC ATA CTG CGT AAT AAG GAG TCT TAA TA
► Phe Ser Thr Phe Ala Asn Ile Leu Arg Asn Lys Glu Ser

21000263604 20219802

Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 43



Title: PROTEASE INHIBITOR
PEPTIDES

Inventor(s): R. Tyler WHITE et al.

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Figure 44

pDD185

α -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TIC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA
►Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG
►Ala Pro Val Asn Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG
►Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT
►Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15A, S17F)

GAA GAA CGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT
►Gu Glu Gly Val Ser Leu Asp Lys Arg Gu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CGG TGC CGT GCA GCT ATC TTC CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT CGA TAG AAG GCG ACC ATG AAA CTG CAG TGA CTT
►Ala Glu Thr Gly Pro Cys Arg Ala Ala Ile Phe Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG
►Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A
►Thr Glu Gu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

100076604 - Dec 1986

Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 45

Plasma kallikrein inhibition by KPI (-4-57) variants

<u>Variant</u>		<u>Substitution</u>			<u>K_i(nM)</u>
		15	16	17	
TW113	KPI (-4-57)				45.00
DD185	KPI (-4-57; M15A, S17F)	A		F	0.39
TW6165	KPI (-4-57; M15A, S17W)	A		W	0.65
TW6166	KPI (-4-57; M15A, S17Y)	A		Y	0.40
TW6175	KPI (-4-57; M15L, S17F)	L		F	0.50
BG028	KPI (-4-57; M15L, S17Y)	L		Y	1.10
TW6183	KPI (-4-57; I16H, S17F)		H	F	1.20
TW6184	KPI (-4-57; I16H, S17Y)		H	Y	0.91
TW6185	KPI (-4-57; I16H, S17W)		H	W	1.30
TW6173	KPI (-4-57; M15A, I16H)	A	H		1.00
TW6174	KPI (-4-57; M15L, I16H)	L	H		0.90

FIGURE 46A

2016 T20 " 410595 C001

Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Variant	Sequence	Inhibition Ki (nM)		
		kallikrein	Plasmin	XIIa
Aprotinin	RPDFCLEPPPTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKRNPNPKSAEDCMRRTCGGA	20.00	0.23	5000.0
Aprotinin R15, S42	DFCLEPPPTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	0.91	0.17	3983.0
KP1 (-4-57)	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	45.00	34.00	3718.0
TW6167	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	61.00	3641.0	161.0
BG031	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	34.00		288.0
BG032	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	49.00		498.0
TW101	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	2000.00	11.50	731.0
TW6208	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA			369.0
TW106	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	560.00	3.70	
DD108	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	1.70	11.20	1600.0
DD109	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	9.50		1681.0
DD110	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	2.10		624.0
DD111	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	5.60		55.0
DD112	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	6.80		998.0
TW6179	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	78.00		368.0
TW6163	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	4.70	103.58	4532.0
TW6172	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	315.00		1463.0
TW6180	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	70.00		885.0
TW6181	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	150.00		39.0
BG001	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	38.00	10.00	1514.0
TW116	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	145.00	89.00	
DD102	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	16.00		315.0
DD103	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	17.00		2128.0
DD104	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	15.00		237.0
DD105	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	18.00		345.0
TW6168	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	25.80		198.0
TW6182	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	36.00		320.0
TW6194	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	70.83		
TW6210	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	54.00		277.0
CL006	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA	110.20		89600.0
BG012	EVVREVCSEQEQTGPKCKARIIRYFYNAKAGLQQTFFVYGGCRAKSNNFFKSAEDCMRRTCGGA		40.0	133.0
				116.0

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FIGURE 46B

Inventor(s): R. Tyler WHITE et al.
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TW6209	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	81.00	45.90	184.0	613.0
TW6211	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	184.00		402.0	
DD128	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	44.00		37.0	
TW6142	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	18.00	18.00	7972.0	225.0
AL301	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	216.00		1557.0	
AL302	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	39.00		316.0	
TW6147	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	35.00		1090.0	179.0
TW6138	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	18.00		921.0	309.0
TW6154	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	11.00		915.0	39.0
TW6155	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	11.00		27.0	
TW6140	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	35.00		475.0	
TW6156	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI				
TW6141	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	42.00			
TW118	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	6.00	24.00	13009.0	68.0
DD100	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	15.00			
TW6157	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	40.00		511.0	168.0
TW6158	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	29.00			
TW6159	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	17.00			64.0
TW6161	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	7.50	18.00	1507.0	8.7
DD101	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	64.00		924.0	
TW6151	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	163.00		1162.0	954.0
TW6139	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	19.00	22.80	152.0	78.0
TW6153	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	11.20	21.30	65.0	36.0
TW122	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	32.00	27.00		581.0
TW6178	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	16.00		444.0	
TW6148	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	40.00			
TW124	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	64.00	48.00		
TW6149	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	54.00			
TW6173	EVVREVCSEQAETGPCRAAHSRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	1.00	7.24	1432.0	
TW6174	EVVREVCSEQAETGPCRALHSRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	0.90	6.89	2796.0	
BG002	EVVREVCSEQAETGPCRALLSRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	0.98	19.00	403.0	60.0
DD129	EVVREVCSEQAETGPCRALFSRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	3.60		1864.0	6.0
DD185	EVVREVCSEQAETGPCRAAIFRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAI	0.39	8.71	150.0	196.0

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Inventor(s): R. Tyler WHITE et al.
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FIGURE 46C

TW6165	EVVREVCSESEQAETGPCKRAIIRWYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	0.65	16.40	206.0		
TW6166	EVVREVCSESEQAETGPCKRAIYRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	0.4	10.10	73.0		
BG028	EVVREVCSESEQAETGPCKRALIYRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	1.10	12.10	93.8		
TW6169	EVVREVCSESEQAETGPCKRALIIRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	1.20		619.0	111.0	
DD113	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	0.85	12.80	293.0	74.0	
TW6175	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	0.50	7.46	35.0	56.0	
TW6201	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	34.60		419.0		
TW6202	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	128.50		1237.0		
TW6203	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	31.20		5045.0		
TW6204	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI			147.0	87.0	
TW6205	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI			195.0	29.0	
DD114	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	0.70	7.77	224.0		
TW6190	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	0.83	52.20	589.0	1396.0	
TW6183	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	1.20	11.68	12440.0	159.0	
TW6184	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	0.91	11.96	14000.0	214.0	
TW6185	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	1.30	18.60	388.0	473.0	
BG003	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	36.00		467.0		
TW6186	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	0.48	8.86	186.0	11.0	
TW6187	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	3.80	15.40	92.0	15.0	
TW6188	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	4.00		419.0	24.0	
TW6189	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	4.00			34.0	
TW6170	EVVREVCSESEQAEPGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	2.50			452.0	
DD115	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI				213.0	299.0
DD170	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	0.99	18.00	550.0		
TW6176	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	3.50	118.00	56.0		
TW6177	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	7.20	32.70	245.0	156.0	
BG006	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	0.30	12.10	80.0		
DD130	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	5.50			9.5	
DD131	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	7.90	2.00	1385.0	3.3	
DD132	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	112.00			16.8	
DD120	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	8.30			11.0	
DD121	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	19.00			21.0	
BG014	EVVREVCSESEQAETGPCKRALIIPRKYFDVTEGKCAPFFYGGCGNRRNNFDTEYCMAVCGSAI	9.20	18.70	18.0		

FIGURE 46D

DD122	EVVREVCSEQAETGPCKRALIIPAWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	15.00			46.0
BCG015	EVVREVCSEQAETGPCKRALIYHWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	6.00	12.20	19.4	597.0
BCG020	EVVREVCSEQAETGPCKRALIHWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	1.70		106.0	
BCG022	EVVREVCSEQAETGPCKRALIHWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	0.64	7.26	14.5	
BCG023	EVVREVCSEQAETGPCKRALIYHWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	23.00		262.0	
BCG024	EVVREVCSEQAETGPCKRALIYHWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	4.10	7.47	38.7	
BCG027	EVVREVCSEQAETGPCKRALIYHWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	5.80		144.0	
DD116	EVVREVCSEQAETGPCKRALIYHWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	0.14		583.0	84.0
TW6191	EVVREVCSEQAETGPCKRALIYHWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	0.26		664.0	20.0
DD117	EVVREVCSEQAETGPCKRALIYHWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	0.11		1034.0	99.0
BCG029	EVVREVCSEQAEVGPCKRALIYHWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	3.20		7.9	
BCG030	EVVREVCSEQAESGPCKRALIYHWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	4.60		26.1	
BCG033	EVVREVCSEQAEVGPCKRALIYHWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	0.75		5.6	
BCG034	EVVREVCSEQAESGPCKRALIYHWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	0.47		18.5	
BCG040	EVVREVCSEQAEGPCKRALIYHWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	3.40		8.6	
BCG016	EVVREVCSEQAETGPCKRGAIYHWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	160.00		178.0	
BCG017	EVVREVCSEQAETGPCKRGAIYHWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	180.00		200.0	
BCG021	EVVREVCSEQAETGPCKRGSIYHWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	340.00		224.0	
BCG025	EVVREVCSEQAETGPCKRGLIYHWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	65.00		16.2	
BCG026	EVVREVCSEQAETGPCKRGAIYHWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	50.00		34.9	
DD118	EVVREVCSEQAETGPCKRALHNRYWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	0.53			
DD134	EVVREVCSEQAETGPCKRALFKRWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	1.10	1.05	15640.0	0.6
DD135	EVVREVCSEQAETGPCKRALFKRWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	1.30		7473.0	0.9
DD136	EVVREVCSEQAETGPCKRALFKRWYFDVTEGKCAPFFFYGGCGGNRNNNFDTEEYCKAVCGSAI	1.10		1.8	

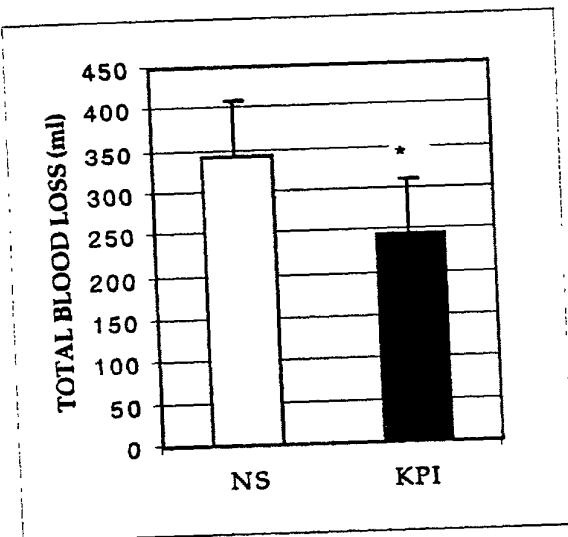
Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 47

VOLUMES

NS	344.25
KPI	245.75

KPI	NS
298	366
266	342
354	294
258	385
168	288
266	469
172	338
184	272
MEAN	245.75
STDEV	66.2414415
TTEST	63.97488346
	0.009094999



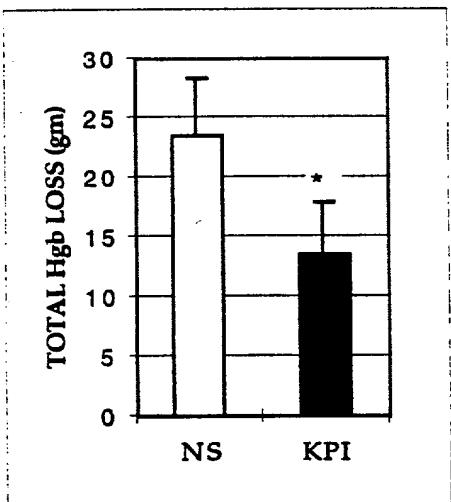
Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 48

HEMOGLOBIN

NS	23.61
KPI	13.59

KPI	NS
16.58	24.95
15.19	24.87
20.21	20.46
8.99	27.59
14.63	18.23
15.31	31.59
7.7	23.26
10.14	17.96
MEAN	13.59375 23.61375
STDEV	4.261438 4.68761
TTEST	0.000536



Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 09/201,715

Figure 49

PaO₂

Baseline PaO ₂		End CPB		Obs 60 min		Obs 180 min	
KPI	NS	KPI	NS	KPI	NS	KPI	NS
652.2	670.9	495.7	60.5	483.7	441.3	391.3	
654	559.2	444.6	132.2	330.1	448.7	264.1	484.6
596.2	622.9	170.2	93.8	415.4	85.1	416.5	81.3
606.2	689.2	264.2	333.9	430.2	529.6	361.9	333.2
633.1	665.1	567.2	341.7	613	568.3	90.8	546.6
646.6	527	507.4	226.9	564.3	438.1	518.2	485.3
563.2	461.7	547.1	89.1	501	42.6	494.2	45.6
659.9	508	416.6	59.7	504.5	405.8	452	383.7
MEAN	626.425	588	426.625	167.225	480.275	369.938	371.1
STDEV	34.4692	85.5055	140.474	117.993	88.6187	196.523	150.277
	3	6	1	1	9	5	4
TTEST	<i>p</i> =	0.268	<i>p</i> =	0.0014	<i>p</i> =	0.17915	<i>p</i> =
	NS.			NS.			

Figure 50

Summary of Data

Total Volumes			Serial Chest tube Hbg		
Total volume loss	Total Hgb Loss	Chest tube Sacrifice	0-30min	30-60min	60-120min
KPI-1 298	16.58	185	113	3.7	4.3
KPI-2 266	15.19	198	68	4.3	6.4
KPI-3 354	20.21	142	212	4.1	4.4
KPI-4 258	8.99	190	68	2.8	4
KPI-5 168	14.63	96	72	6.3	6.5
KPI-6 266	15.31	188	78	4.1	6.1
KPI-7 172	7.7	134	38	3.1	4.6
KPI-8 184	10.14	158	26	6.9	5.8
MEAN	245.75	13.59	MEAN	4.41	5.26
STDEV	66.24	4.26	STDEV	1.45	1.04
NS-1A 366	24.95	274	92	7.7	8.6
NS-2 342	24.87	236	106	7.2	7.4
NS-3 294	20.46	252	42	5.4	7.5
NS-4 385	27.59	303	82	8.4	7.2
NS-5 288	18.23	140	148	7.5	7.2
NS-6 469	31.59	261	208	4	7
NS-7 338	23.26	218	120	7.5	7.7
NS-8 272	17.96	206	66	7.4	8.2
MEAN	344.25	23.61	MEAN	6.89	7.6
STDEV	63.97	4.69	STDEV	1.44	1.04

*p = 0.009

*p = 0.0005

*p = 0.004 *p = 0.002

NS

NS